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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,433	08/10/2000	Mark C. Noe	PC10491A	6255

7590 06/10/2003

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EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	18

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,433	NOE ET AL.	
	Examin r	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to an RCE filed on 3/14/03. There are five claims pending and four under consideration. Claims 16-20 are use claims. This is the third action on the merits. The application concerns some uses of aggrecanase inhibitors having a carboxylic acid hydroxamide functional group.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/14/03 has been entered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as reasonably to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. What are the

chemical structures of the aggrecanase inhibitors whose use Applicants claim? Beyond molecular weight, the presence of a single functional group, and a desired pharmacological activity, Applicants do not demonstrate that they understand the structures of these molecules. According to the MPEP § "[a]n applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, **structures** [emphasis added], figures, diagrams, and **formulas** [emphasis added], that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or **structural chemical formulas** [emphasis added], that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). "Compliance with the written description requirement is essentially a fact-

based inquiry that will necessarily vary depending on the nature of the invention claimed. '" *Enzo Biochem*, 296 F.3d at 1324, 63 USPQ2d at 1613." Applicants limited structural information is not sufficient to distinguish their compounds.

4. Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compounds of Formula I on page 5, does not reasonably provide enablement for making all the carboxylic acid hydroxamides with the desired aggrecanase activity they intend to use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Since Applicants do not specify the structures of the compounds they intend to use, how can the skilled process chemist be expected to make these compounds? Directions to the pharmacologist for how to seek such compounds hardly constitute directions to the chemist of how to make them.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*,

230 USPQ 546. a) Making any particular substrate would require ascertaining its chemical structure, devising a synthesis of the compound, and successfully preparing the substance in the laboratory. Since there is no direction concerning the first step, no degree of experimentation would be sufficient to perform this task. b) The direction concerning compound synthesis is found in the passage spanning line 14, page 21 through line 15, page 50. This passage concerns only synthesis of compounds of formula I. There is no direction concerning the synthesis of any other compounds meeting Applicants claim limitations. c) There are working examples of synthesis of compound of formula (I) in the passage spanning line 1, page 65 to line 32, page 82. There are no working examples of synthesis of compounds not fitting formula I. d) The nature of the invention requires both chemical synthesis, which involves chemical reactions, and therapeutic activity. e) The state of the art is summarized in pages 1-4 of the specification. f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. h) The breadth of the claims includes the six diseases mentioned in claim 16 as well as the presently unknown list of compounds embraced by claim 16.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before

November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson ('361). The compounds of this reference, which are taught in the passage spanning line 1, column 3 through line 65, column 5 all possess the required carboxylic acid hydroxamide functional group. The compounds are all less than 2000 molecular weight. Lines 35-61, column 6 teach treatment of a number of conditions including osteoarthritis with the compounds of this reference. Claim 15 of the reference is drawn to these therapeutic uses. The passage spanning line 66, column 1 to line 6 column 2 of this reference teaches aggrecanase inhibitory activity. The reference is silent as to the potencies of aggrecanase enzyme inhibition of the disclosed compounds. The testing method is taught by the references but without results. For all the Examiner knows, the compounds taught in Robinson ('361) do have the required potency.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed

but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

6. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Reiter ('392). The compounds of this reference, which are taught in the passage spanning line 35, column 3 through line 20, column 4 all possess the required carboxylic acid hydroxamide functional group. The compounds are all less than 2000 molecular weight. The passage spanning line 58, column 5 through line 17, column 6 teach treatment of a number of conditions including osteoarthritis with the compounds of this reference. Claim 7 of the reference is drawn to these therapeutic uses. Lines 1-8, column 1 of this reference teaches aggrecanase inhibitory activity. The reference is silent as to the potencies of aggrecanase enzyme inhibition of the disclosed compounds. The testing method is taught by the references but without results. For all the Examiner knows, the compounds taught in Reiter ('392) do have the required potency.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed

but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

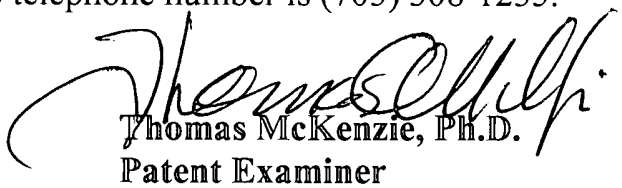
7. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Duan ('336). The compounds of this reference, which are taught in the passage spanning line 41, column 76 through line 56, column 237 all possess the required carboxylic acid hydroxamide functional group. The compounds are all less than 2000 molecular weight. Lines 23-49, column 22 teach treatment of a number of conditions including osteoarthritis and psoriasis with the compounds of this reference. Lines 43-46, column 238 of this reference teaches aggrecanase inhibitory activity. The reference is silent as to the potencies of aggrecanase enzyme inhibition of the disclosed compounds. The testing method is taught by the references but without results. For all the Examiner knows, the compounds taught in Duan ('336) do have the required potency.

8. Claims 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bender ('653). The compounds of this reference, which are taught in the passage spanning line 13, column 3 through line 52, column 4 all possess the required carboxylic acid hydroxamide functional group. The compounds are all less than 2000 molecular weight. Lines 7-16, column 2 teach treatment of a number of

conditions including osteoarthritis with the compounds of this reference. Bender ('653) is understandably silent about aggrecanase because aggrecanase was not known at the effective date of filing of this reference. For all the Examiner knows, the compounds taught in Bender ('653) do have the required potency.

Conclusion

9. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.



Thomas McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK
June 4, 2003